Autism genes are in all of us, new research reveals

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Quinn, an autistic boy, and the line of toys he made before falling asleep. Repeatedly stacking or lining up objects is a behavior commonly associated with autism. Credit: Wikipedia.

New light has been shed on the genetic relationship between autistic spectrum disorders (ASD) and ASD-related traits in the wider population, by a team of international researchers including academics from the University of Bristol, the Broad Institute of Harvard and MIT,

and Massachusetts General Hospital (MGH).

The researchers studied whether there is a genetic relationship between ASD and the expression of ASD-related traits in populations not considered to have ASD. Their findings, published this week in *Nature Genetics*, suggest that genetic risk underlying ASD, including both inherited variants and de novo influences (not seen in an individual's parents), affects a range of behavioural and developmental traits across the population, with those diagnosed with ASD representing a severe presentation of those traits.

Autism spectrum disorders are a class of neurodevelopmental conditions affecting about 1 in 100 children. They are characterised by social interaction difficulties, communication and language impairments, as well as stereotyped and repetitive behaviour. These core symptoms are central to the definition of an ASD diagnosis but also occur, to varying degrees, in unaffected individuals and form an underlying behavioural continuum.

With recent advances in genome sequencing and analysis, a picture of ASD's genetic landscape has started to take shape. Research has shown that most ASD risk is polygenic (stemming from the combined small effects of thousands of genetic differences, distributed across the genome). Some cases are also associated with rare genetic variants of large effect, which are usually de novo.

"There has been a lot of strong but indirect evidence that has suggested these findings," said Dr Mark Daly, co-director of the Broad Institute's Medical and Population Genetics (MPG) Program and senior author of the study.

"Once we had measurable genetic signals in hand - both polygenic risk and specific de novo mutations known to contribute to ASD - we were

able to make an incontrovertible case that the genetic risk contributing to autism is genetic risk that exists in all of us, and influences our behaviour and social communication."

Study co-first author Dr Elise Robinson, from MGH, said: "We can use behavioural and cognitive data in the general population to untangle the mechanisms through which different types of genetic risk are operating. We now have a better path forward in terms of expecting what types of disorders and traits are going to be associated with certain types of genetic risk."

"Our study shows that collecting and using phenotypic and genetic data in typically developing children can be useful in terms of the design and interpretation of studies targeting complex neurodevelopmental and psychiatric disorders," said study co-first author Dr Beate St Pourcain, from the Medical Research Council Integrative Epidemiology Unit at the University of Bristol and the Max Planck Institute for Psycholinguistics.

"Based on the genetic link between population-based social-communication difficulties and clinical ASD, we may now gain further phenotypic insight into a defined set of genetically-influenced ASD symptoms. This may help us to identify and investigate biological processes in typically-developing children, which are disturbed in children with ASD."

The data on unaffected individuals came from a general population cohort (the Bristol-based Avon Longitudinal Study of Parents and Children) and a nuclear family cohort (the Simons Simplex Collection) of ASD cases and unaffected siblings; ASD collections included several large, international autism genetic studies: the Psychiatric Genomics Consortium Autism group, the iPSYCH autism project in Denmark, the SSC, and the Autism Sequencing Consortium.

Professor George Davey Smith, co-author and scientific director of ALSPAC, said: "Many traits that related to disease risk - like blood pressure or cholesterol levels - demonstrate a similar continuum of risk, with contributions from common and rare genetic variants, plus environmental and chance events. The present study demonstrates how this continuum applies to a condition generally thought of as either existing or not."

The researchers expect the approach to be used to explore the associations between genetic risk and behavioural traits in other neuropsychiatric disorders such as schizophrenia in the future.

More information: 'Genetic risk for autism spectrum disorders and neuropsychiatric variation in the general population' by Robinson, EB, St. Pourcain, B et al in Nature Genetics. Online March 21, 2016. DOI: 10.1038/ng.3529

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